



#4

1

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<120> MODIFICATIONS OF THE VEGF RECEPTOR-2 PROTEIN AND
METHODS OF USE

<130> 0125-0016US

<140> 09/390,326

<141> 1999-09-07

<160> 12

<170> PatentIn Ver. 2.0

<210> 1

<211> 31

<212> DNA

<213> Homo sapiens

<400> 1

cagcatatgg atccagatga actcccattg g

31

<210> 2

<211> 34

<212> DNA

<213> Homo sapiens

<400> 2

gcggtcgact taaacaggag gagagctcag tgtg

34

<210> 3

<211> 33

<212> DNA

<213> Homo sapiens

<400> 3

gcacatatgg aacgactgcc ttatgatgcc agc

33

<210> 4

<211> 38

<212> DNA

<213> Homo sapiens

<400> 4

cctgtcgact tatccagaat cctcttccat gctcaaag

38

<210> 5
 <211> 317
 <212> PRT
 <213> Homo sapiens

<400> 5

Met	Asp	Pro	Asp	Glu	Leu	Pro	Leu	Asp	Glu	His	Cys	Glu	Arg	Leu	Pro	1	5	10	15
Tyr	Asp	Ala	Ser	Lys	Trp	Glu	Phe	Pro	Arg	Asp	Arg	Leu	Lys	Leu	Gly	20	25	30	
Lys	Pro	Leu	Gly	Arg	Gly	Ala	Phe	Gly	Gln	Val	Ile	Glu	Ala	Asp	Ala	35	40	45	
Phe	Gly	Ile	Asp	Lys	Thr	Ala	Thr	Cys	Arg	Thr	Val	Ala	Val	Lys	Met	50	55	60	
Leu	Lys	Glu	Gly	Ala	Thr	His	Ser	Glu	His	Arg	Ala	Leu	Met	Ser	Glu	65	70	75	80
Leu	Lys	Ile	Leu	Ile	His	Ile	Gly	His	His	Leu	Asn	Val	Val	Asn	Leu	85	90	95	
Leu	Gly	Ala	Cys	Thr	Lys	Pro	Gly	Gly	Pro	Leu	Met	Val	Ile	Val	Glu	100	105	110	
Phe	Cys	Lys	Phe	Gly	Asn	Leu	Ser	Thr	Tyr	Leu	Arg	Ser	Lys	Arg	Asn	115	120	125	
Glu	Phe	Val	Pro	Tyr	Lys	Glu	Ala	Pro	Glu	Asp	Leu	Tyr	Lys	Asp	Phe	130	135	140	
Leu	Thr	Leu	Glu	His	Leu	Leu	Ile	Cys	Tyr	Ser	Phe	Gln	Val	Ala	Lys	145	150	155	160
Gly	Met	Glu	Phe	Leu	Ala	Ser	Arg	Lys	Cys	Ile	His	Arg	Asp	Leu	Ala	165	170	175	
Ala	Arg	Asn	Ile	Leu	Leu	Ser	Glu	Lys	Asn	Val	Val	Lys	Ile	Cys	Asp	180	185	190	
Phe	Gly	Leu	Ala	Arg	Asp	Ile	Tyr	Lys	Asp	Pro	Asp	Tyr	Val	Arg	Lys	195	200	205	
Gly	Asp	Ala	Arg	Leu	Pro	Leu	Lys	Trp	Met	Ala	Pro	Glu	Thr	Ile	Phe	210	215	220	
Asp	Arg	Val	Tyr	Thr	Ile	Gln	Ser	Asp	Val	Trp	Ser	Phe	Gly	Val	Leu	225	230	235	240
Leu	Trp	Glu	Ile	Phe	Ser	Leu	Gly	Ala	Ser	Pro	Tyr	Pro	Gly	Val	Lys	245	250	255	
Ile	Asp	Glu	Glu	Phe	Cys	Arg	Arg	Leu	Lys	Glu	Gly	Thr	Arg	Met	Arg	260	265	270	

Ala Pro Asp Tyr Thr Thr Pro Glu Met Tyr Gln Thr Met Leu Asp Cys
275 280 285

Trp His Gly Glu Pro Ser Gln Arg Pro Thr Phe Ser Glu Leu Val Glu
290 295 300

His Leu Gly Asn Leu Leu Gln Ala Asn Ala Gln Gln Asp
305 310 315

<210> 6

<211> 386

<212> PRT

<213> E. coli

<400> 6

Asp Pro Met Gln Leu Pro Tyr Asp Ser Arg Trp Glu Phe Pro Arg Asp
1 5 10 15

Gly Leu Val Leu Gly Arg Val Leu Gly Ser Gly Ala Phe Gly Lys Val
20 25 30

Val Glu Gly Thr Ala Tyr Gly Leu Ser Arg Ser Gln Pro Val Met Lys
35 40 45

Val Ala Val Lys Met Leu Lys Pro Thr Ala Arg Ser Ser Glu Lys Gln
50 55 60

Ala Leu Met Ser Glu Leu Lys Ile Met Thr His Leu Gly Pro His Leu
65 70 75 80

Asn Ile Val Asn Leu Leu Gly Ala Cys Thr Lys Ser Gly Pro Ile Tyr
85 90 95

Ile Ile Thr Glu Tyr Cys Phe Tyr Gly Asp Leu Val Asn Tyr Leu His
100 105 110

Lys Asn Arg Asp Ser Phe Leu Ser His His Pro Glu Lys Pro Lys Lys
115 120 125

Glu Leu Asp Ile Phe Gly Leu Asn Pro Ala Asp Glu Ser Thr Arg Ser
130 135 140

Tyr Val Ile Leu Ser Phe Glu Asn Asn Gly Asp Tyr Met Asp Met Lys
145 150 155 160

Gln Ala Asp Thr Thr Gln Tyr Val Pro Met Leu Glu Arg Lys Glu Val
165 170 175

Ser Lys Tyr Ser Asp Ile Gln Arg Ser Leu Tyr Asp Arg Pro Ala Ser
180 185 190

Tyr Lys Lys Lys Ser Met Leu Asp Ser Glu Val Lys Asn Leu Leu Ser
195 200 205

Asp Asp Asn Ser Glu Gly Leu Thr Leu Leu Asp Leu Leu Ser Phe Thr
210 215 220

Tyr Gln Val Ala Arg Gly Met Glu Phe Leu Ala Ser Lys Asn Cys Val
225 230 235 240

His Arg Asp Leu Ala Ala Arg Asn Val Leu Leu Ala Gln Gly Lys Ile
245 250 255

Val Lys Ile Cys Asp Phe Gly Leu Ala Arg Asp Ile Met His Asp Ser
260 265 270

Asn Tyr Val Ser Lys Gly Ser Thr Phe Leu Pro Val Lys Trp Met Ala
275 280 285

Pro Glu Ser Ile Phe Asp Asn Leu Tyr Thr Thr Leu Ser Asp Val Trp
290 295 300

Ser Tyr Gly Ile Leu Leu Trp Glu Ile Phe Ser Leu Gly Gly Thr Pro
305 310 315 320

Tyr Pro Gly Met Met Val Asp Ser Thr Phe Tyr Asn Lys Ile Lys Ser
325 330 335

Gly Tyr Arg Met Ala Lys Pro Asp His Ala Thr Ser Glu Val Tyr Glu
340 345 350

Ile Met Val Lys Cys Trp Asn Ser Glu Pro Glu Lys Arg Pro Ser Phe
355 360 365

Tyr His Leu Ser Glu Ile Val Glu Asn Leu Leu Pro Gly Gln Tyr Lys
370 375 380

Lys Ser
385

<210> 7

<211> 310

<212> PRT

<213> Homo sapiens

<400> 7

Met Leu Ala Gly Val Ser Glu Tyr Glu Leu Pro Glu Asp Pro Arg Trp
1 5 10 15

Glu Leu Pro Arg Asp Arg Leu Val Leu Gly Lys Pro Leu Gly Glu Gly
20 25 30

Cys Phe Gly Gln Val Val Leu Ala Glu Ala Ile Gly Leu Asp Lys Asp
35 40 45

Lys Pro Asn Arg Val Thr Lys Val Ala Val Lys Met Leu Lys Ser Asp
50 55 60

Ala Thr Glu Lys Asp Leu Ser Asp Leu Ile Ser Glu Met Glu Met Met
65 70 75 80

Lys Met Ile Gly Lys His Lys Asn Ile Ile Asn Leu Leu Gly Ala Cys
85 90 95

Thr Gln Asp Gly Pro Leu Tyr Val Ile Val Glu Tyr Ala Ser Lys Gly
 100 105 110
 Asn Leu Arg Glu Tyr Leu Gln Ala Arg Arg Pro Pro Gly Leu Glu Tyr
 115 120 125
 Cys Tyr Asn Pro Ser His Asn Pro Glu Glu Gln Leu Ser Ser Lys Asp
 130 135 140
 Leu Val Ser Cys Ala Tyr Gln Val Ala Arg Gly Met Glu Tyr Leu Ala
 145 150 155 160
 Ser Lys Lys Cys Ile His Arg Asp Leu Ala Ala Arg Asn Val Leu Val
 165 170 175
 Thr Glu Asp Asn Val Met Lys Ile Ala Asp Phe Gly Leu Ala Arg Asp
 180 185 190
 Ile His His Ile Asp Tyr Tyr Lys Lys Thr Thr Asn Gly Arg Leu Pro
 195 200 205
 Val Lys Trp Met Ala Pro Glu Ala Leu Phe Asp Arg Ile Tyr Thr His
 210 215 220
 Gln Ser Asp Val Trp Ser Phe Gly Val Leu Leu Trp Glu Ile Phe Thr
 225 230 235 240
 Leu Gly Gly Ser Pro Tyr Pro Gly Val Pro Val Glu Glu Leu Phe Lys
 245 250 255
 Leu Leu Lys Glu Gly His Arg Met Asp Lys Pro Ser Asn Cys Thr Asn
 260 265 270
 Glu Leu Tyr Met Met Met Arg Asp Cys Trp His Ala Val Pro Ser Gln
 275 280 285
 Arg Pro Thr Phe Lys Gln Leu Val Glu Asp Leu Asp Arg Ile Val Ala
 290 295 300
 Leu Thr Ser Asn Gln Glu
 305 310

<210> 8
 <211> 297
 <212> PRT
 <213> Homo sapiens

<400> 8
 Val Phe Pro Cys Ser Val Tyr Val Pro Asp Glu Trp Glu Val Ser Arg
 1 5 10 15
 Glu Lys Ile Thr Leu Leu Arg Glu Leu Gly Gln Gly Ser Phe Gly Met
 20 25 30
 Val Tyr Glu Gly Asn Ala Arg Asp Ile Ile Lys Gly Glu Ala Glu Thr
 35 40 45

Arg Val Ala Val Lys Thr Val Asn Glu Ser Ala Ser Leu Arg Glu Arg
50 55 60

Ile Glu Phe Leu Asn Glu Ala Ser Val Met Lys Gly Phe Thr Cys His
65 70 75 80

His Val Val Arg Leu Leu Gly Val Val Ser Lys Gly Gln Pro Thr Leu
85 90 95

Val Val Met Glu Leu Met Ala His Gly Asp Leu Lys Ser Tyr Leu Arg
100 105 110

Ser Leu Arg Pro Glu Ala Glu Asn Asn Pro Gly Arg Pro Pro Pro Thr
115 120 125

Leu Gln Glu Met Ile Gln Met Ala Ala Glu Ile Ala Asp Gly Met Ala
130 135 140

Tyr Leu Asn Ala Lys Lys Phe Val His Arg Asp Leu Ala Ala Arg Asn
145 150 155 160

Cys Met Val Ala His Asp Phe Thr Val Lys Ile Gly Asp Phe Gly Met
165 170 175

Thr Arg Asp Ile Tyr Glu Thr Asp Tyr Tyr Arg Lys Gly Gly Lys Gly
180 185 190

Leu Leu Pro Val Arg Trp Met Ala Pro Glu Ser Leu Lys Asp Gly Val
195 200 205

Phe Thr Thr Ser Ser Asp Met Trp Ser Phe Gly Val Val Leu Trp Glu
210 215 220

Ile Thr Ser Leu Ala Glu Gln Pro Tyr Gln Gly Leu Ser Asn Glu Gln
225 230 235 240

Val Leu Lys Phe Val Met Asp Gly Gly Tyr Leu Asp Gln Pro Asp Asn
245 250 255

Cys Pro Glu Arg Val Thr Asp Leu Met Arg Met Cys Trp Gln Phe Asn
260 265 270

Pro Asn Met Arg Pro Thr Phe Leu Glu Ile Val Asn Leu Leu Lys Asp
275 280 285

Asp Leu His Pro Ser Phe Pro Glu Val
290 295

<210> 9

<211> 367

<212> PRT

<213> Homo sapiens

<400> 9

Met Asp Pro Asp Glu Val Pro Leu Asp Glu Gln Cys Glu Arg Leu Pro
1 5 10 15

Tyr Asp Ala Ser Lys Trp Glu Phe Ala Arg Glu Arg Leu Lys Leu Gly
 20 25 30
 Lys Ser Leu Gly Arg Gly Ala Phe Gly Lys Val Val Gln Ala Ser Ala
 35 40 45
 Phe Gly Ile Lys Lys Ser Pro Thr Cys Arg Thr Val Ala Val Lys Met
 50 55 60
 Leu Lys Glu Gly Ala Thr Ala Ser Glu Tyr Lys Ala Leu Met Thr Glu
 65 70 75 80
 Leu Lys Ile Leu Thr His Ile Gly His His Leu Asn Val Val Asn Leu
 85 90 95
 Leu Gly Ala Cys Thr Lys Gln Gly Gly Pro Leu Met Val Ile Val Glu
 100 105 110
 Tyr Cys Lys Tyr Gly Asn Leu Ser Asn Tyr Leu Lys Ser Lys Arg Asp
 115 120 125
 Leu Phe Phe Leu Asn Lys Asp Ala Ala Leu His Met Glu Pro Lys Lys
 130 135 140
 Glu Lys Met Glu Pro Gly Leu Glu Gln Gly Lys Lys Pro Arg Leu Asp
 145 150 155 160
 Ser Val Thr Ser Ser Glu Ser Phe Ala Ser Ser Gly Phe Gln Glu Asp
 165 170 175
 Lys Ser Leu Ser Asp Val Glu Glu Glu Glu Asp Ser Asp Gly Phe Tyr
 180 185 190
 Lys Glu Pro Ile Thr Met Glu Asp Leu Ile Ser Tyr Ser Phe Gln Val
 195 200 205
 Ala Arg Gly Met Glu Phe Leu Ser Ser Arg Lys Cys Ile His Arg Asp
 210 215 220
 Leu Ala Ala Arg Asn Ile Leu Leu Ser Glu Asn Asn Val Val Lys Ile
 225 230 235 240
 Cys Asp Phe Gly Leu Ala Arg Asp Ile Tyr Lys Asn Pro Asp Tyr Val
 245 250 255
 Arg Lys Gly Asp Thr Arg Leu Pro Leu Lys Trp Met Ala Pro Glu Ser
 260 265 270
 Ile Phe Asp Lys Ile Tyr Ser Thr Lys Ser Asp Val Trp Ser Tyr Gly
 275 280 285
 Val Leu Leu Trp Glu Ile Phe Ser Leu Gly Gly Ser Pro Tyr Pro Gly
 290 295 300
 Val Gln Met Asp Glu Asp Phe Cys Ser Arg Leu Arg Glu Gly Met Arg
 305 310 315 320

Met Arg Ala Pro Glu Tyr Ser Thr Pro Glu Ile Tyr Gln Ile Met Leu
 325 330 335

Asp Cys Trp His Arg Asp Pro Lys Glu Arg Pro Arg Phe Ala Glu Leu
 340 345 350

Val Glu Lys Leu Gly Asp Leu Leu Gln Ala Asn Val Gln Gln Asp
 355 360 365

<210> 10

<211> 30

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Oligonucleotide

<400> 10

ctcagcagga ttgataagac tacattgttc

30

<210> 11

<211> 36

<212> DNA

<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Oligonucleotide

<400> 11

gaatttgtcc cctacaagga agctcctgaa gatctg

36

<210> 12

<211> 367

<212> PRT

<213> Homo sapiens

<400> 12

Met Asp Pro Asp Glu Leu Pro Leu Asp Glu His Cys Glu Arg Leu Pro
 1 5 10 15

Tyr Asp Ala Ser Lys Trp Glu Phe Pro Arg Asp Arg Leu Lys Leu Gly
 20 25 30

Lys Pro Leu Gly Arg Gly Ala Phe Gly Gln Val Ile Glu Ala Asp Ala
 35 40 45

Phe Gly Ile Asp Lys Thr Ala Thr Cys Arg Thr Val Ala Val Lys Met
 50 55 60

Leu Lys Glu Gly Ala Thr His Ser Glu His Arg Ala Leu Met Ser Glu
 65 70 75 80

Leu Lys Ile Leu Ile His Ile Gly His His Leu Asn Val Val Asn Leu
 85 90 95

Leu Gly Ala Cys Thr Lys Pro Gly Gly Pro Leu Met Val Ile Val Glu
 100 105 110
 Phe Cys Lys Phe Gly Asn Leu Ser Thr Tyr Leu Arg Ser Lys Arg Asn
 115 120 125
 Glu Phe Val Pro Tyr Lys Thr Lys Gly Ala Arg Phe Arg Gln Gly Lys
 130 135 140
 Asp Tyr Val Gly Ala Ile Pro Val Asp Leu Lys Arg Arg Leu Asp Ser
 145 150 155 160
 Ile Thr Ser Ser Gln Ser Ser Ala Ser Ser Gly Phe Val Glu Glu Lys
 165 170 175
 Ser Leu Ser Asp Val Glu Glu Glu Glu Ala Pro Glu Asp Leu Tyr Lys
 180 185 190
 Asp Phe Leu Thr Leu Glu His Leu Leu Ile Cys Tyr Ser Phe Gln Val
 195 200 205
 Ala Lys Gly Met Glu Phe Leu Ala Ser Arg Lys Cys Ile His Arg Asp
 210 215 220
 Leu Ala Ala Arg Asn Ile Leu Leu Ser Glu Lys Asn Val Val Lys Ile
 225 230 235 240
 Cys Asp Phe Gly Leu Ala Arg Asp Ile Tyr Lys Asp Pro Asp Tyr Val
 245 250 255
 Arg Lys Gly Asp Ala Arg Leu Pro Leu Lys Trp Met Ala Pro Glu Thr
 260 265 270
 Ile Phe Asp Arg Val Tyr Thr Ile Gln Ser Asp Val Trp Ser Phe Gly
 275 280 285
 Val Leu Leu Trp Glu Ile Phe Ser Leu Gly Ala Ser Pro Tyr Pro Gly
 290 295 300
 Val Lys Ile Asp Glu Glu Phe Cys Arg Arg Leu Lys Glu Gly Thr Arg
 305 310 315 320
 Met Arg Ala Pro Asp Tyr Thr Thr Pro Glu Met Tyr Gln Thr Met Leu
 325 330 335
 Asp Cys Trp His Gly Glu Pro Ser Gln Arg Pro Thr Phe Ser Glu Leu
 340 345 350
 Val Glu His Leu Gly Asn Leu Leu Gln Ala Asn Ala Gln Gln Asp
 355 360 365